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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 265.00450201	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US05/00722	International filing date (*day/month/year*) 10 January 2005 (10.01.2005)	(Earliest) Priority Date (*day/month/year*) 09 January 2004 (09.01.2004)
Applicant BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      ☒ the international application in the language in which it was filed.
      ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box No. II)
3. ☒ **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,
   a. the figure of the drawings to be published with the abstract is Figure No. _____
      ☐ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☐ as selected by this Authority, because this figure better characterizes the invention.
   b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/00722

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1 and 7

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/00722

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/00
US CL : 435/4
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/4

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
medline, cancerlit, biosis, uspatents

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE et al. Regulation of cell movement is mediated by stretch-activated calcium channels. Nature. July 1999, Vol. 400, pages 382-386.	1,7
X	YAO et al. A protein kinase G-sensitive channel mediates flow-induced Ca 2+ entry into vascular endothelial cells. FASEB Journal. May 2000, Vol. 14, pages 932-938.	1

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
01 December 2005 (01.12.2005)

Date of mailing of the international search report
26 JAN 2006

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Form PCT/ISA/210 (second sheet) (April 2005)

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1, 7, drawn to the special technical feature for identifying an agent that decreases activity of a mechanosensitive Ca2+ channel comprising contacting a motile cell expressing said channel with a candidate agent.

Group 2, claim(s) 1-6, 8-10, drawn to the special technical feature for identifying an agent that decreases activity of a mechanosensitive Ca2+ channel (MscCa)comprising contacting a tumor cell expressing the MscCa channel wherein said channel comprises SEQ ID NO:2.

Group 3, claim(s) 11, drawn to the special technical feature of an agent that decreases activity of a MscCa channel.

Group 4, claim(s) 12-18, drawn to the special technical feature for identifying an agent that decreases a phenotype of a cell comprising contacting an MscCa channel with a candidate agent to yield a treated cell.

Group 5, claim(s) 19, drawn to the special technical feature of an agent that decreases the phenotype of a cell that expresses an MscCa channel.

Group 6, claim(s) 20-25, 29-30, drawn to the special technical feature of a method for treating cancer comprising administering a polypeptide agent that decreases the activity of a mechanosensitive ion channel present on cancer cells.

Group 7, claim(s) 20-23, 26-27, 29-30, drawn to the special technical feature of a method for treating cancer comprising administering an antibody that decreases the activity of a mechanosensitive ion channel present on cancer cells.

Group 8, claim(s) 20-23, 28-34, drawn to the special technical feature of a method for treating cancer comprising administering a polynucleotide that decreases expression of a MscCa polypeptide.

The inventions listed as Groups 1-8 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups 1-8 appears to be a method for identifying an agent that decreases activity of a mechanosensitive Ca2+ permeable (MscCa) channel comprising contacting a cell expressing an MscCa channel with a candidate agent wherein decreased activity of an MscCa channel indicates that the candidate agent decreases the activity of an MscCa channel.

However, Yao *et al.* (A protein kinase G-sensitive channel mediates flow-induced Ca2+ enry into vascular endothelial cells, FASEB Journal, May 2000, Vol. 14, pages 932-938) identify a mechanosensitive Ca2+ permeable cation channel and teach that inhibition of this cannel abolished the rise of calcium ions (page 932, second column, last paragraph). Yao *et al.* further identify agents that decrease the activity of said channels in cells compared to controls (page 936, second column).

Therefore, the technical feature linking the inventions of Groups 1-8 does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.